

## **RESPONSE**

### **I. Status of the Claims**

No claims have been cancelled. No claims have been amended. No new claims have been added.

Claims 1-3 and 6-9 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**.

### **II. Rejection of Claims 1-3 and 6-9 Under 35 U.S.C. § 101**

The Action first rejects claims 1-3 and 6-9 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

As set forth in Applicants' response filed on October 28, 2002 ("the previous response") to the First Office Action in this case ("the First Action"), which was mailed on June 28, 2002, a sequence sharing over 90% percent identity at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as "Homo sapiens similar to G protein-coupled receptor 56" (GenBank accession number XM\_169439). In fact, Applicants' sequence appears to be a splice variant of XM\_169439, as the sequences are 100% identical at the protein level with the exception of the extra exon present in the XM\_169439 sequence. The Action states that "there is no sufficient and credible information that indicates the published sequence is a truly functional GPCR" (Action at page 3). Additionally, in the previous response, Applicants invited the Examiner's attention to the fact that a sequence sharing 68% percent identity and 78% similarity at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as "Mus musculus Pb99 gene sequence" (GenBank accession number AF249738). This protein is the murine homolog of the described human sequence, and has been characterized by the same third party scientists as a G-protein coupled receptor (2000, Mol. Cell. Biol. 20:4405-4410). The Action again states that "there is no sufficient and credible information that indicates the published sequence is a truly functional GPCR" (Action at page 4).

As additional evidence of the utility of the presently claimed sequence, Applicants have recently become aware of an additional sequence sharing over 99% percent identity at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by different third party scientists *wholly unaffiliated with Applicants* as “GPR-97” (GenBank accession number NM\_170776). The alignment of these sequences (query is SEQ ID NO:43), the Genbank report for NM\_170776, and the abstract from the Fredriksson *et al.* manuscript cited in the Genbank report, are shown in **Exhibit B**. The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given all of these GenBank annotations, there can be no question that those skilled in the art would clearly believe that Applicants’ sequence is a G-protein coupled receptor. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Thus, as described above, the present application describes a novel G-protein coupled receptor (GPCR). However, the Action once again questions prediction of protein function based upon protein homology, citing the same articles cited in the First Action, specifically, Bork and Koonin (1998, *Nature Genetics* 18:313-318; “Bork and Koonin”), Ji *et al.* (1998, *J. Biol. Chem.* 273:17299-17302; “Ji”) and Yan *et al.* (2000, *Science* 290:523-527; “Yan”). Unfortunately, and improperly, the Examiner merely dismisses Applicants remarks concerning the shortcomings of these articles as set forth in the previous response, and simply restates the exact same comments regarding the teachings of these references, without specifically addressing Applicants comments. Therefore, Applicants will again set forth the shortcomings of these articles, and point out the failure of these articles to support the alleged lack of utility of the presently claimed sequence.

First, with regard to the Bork and Koonin article, Bork and Koonin themselves conclude “(i)n summary, the currently available methods for sequence analysis are sophisticated, and while further improvements will certainly ensue, they are already capable of extracting subtle but functionally relevant signals from protein sequences (Bork and Koonin, page 317). Thus, the Bork and Koonin article is hardly indicative of a high level of uncertainty in assigning function based on sequence, and thus does not support the alleged lack of utility.

With regard to Ji, an exact quote from Ji completely undermines the question of asserted utility

based upon protein homology: “a substantial degree of amino acid homology is found between members of a particular subfamily, but comparisons between subfamilies show significantly less or no similarity” (Ji at 17299, first paragraph, emphasis added). This quote suggests that homology with members of a G-protein coupled receptor is indicative that the particular sequence is in fact a member of that subfamily - the fact that there is little or no homology between subfamilies is completely irrelevant. Thus, Ji does not support the alleged lack of utility.

Furthermore, regarding Yan, this paper cites only one example, two isoforms of the anhidrotic ectodermal dysplasia (EDA) gene, where a two amino acid change conforms one isoform (EDA-A1) into the second isoform (EDA-A2). However, while it is true that this amino acid change results in binding to different receptors, it is important to note that the different receptors bound by the two isoforms are in fact related (Yan at page 523). Furthermore, the EDA-A2 receptor was correctly identified as a member of the tumor necrosis factor receptor superfamily based solely on sequence similarity (Yan at page 523). Thus, Yan does not suggest a high level of uncertainty in assigning function based on sequence, and thus also does not support the alleged lack of utility.

The Action again states that “significant further research” (Action at page 6) is needed to practice the claimed invention. Applicants pointed out in the previous response that, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit’s holding in *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), “*Brana*”), which clearly states that “pharmaceutical inventions, necessarily includes the expectation of further research and development” (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is “undue”, not “experimentation”. *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra; Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Furthermore, Applicants point out that significant commercial exploitation of nucleic acid

sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling (see below) to chromosomal mapping (see below) are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and thus directly contradicts the Examiner's allegation that "significant further research" is required to practice the claimed invention.

The Action also questions the applicability of the case law cited by Applicants in the previous response, stating that "the Response cites a device case law" and "(t)hus, applicants' argument citing a case law regarding a device is irrelevant to the instant case" (Action at page 5). Section 101 of the Patent Act of 1952, 35 U.S.C. § 101, provides that "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof," may obtain a patent on the invention or discovery. Applicants point out that 35 U.S.C. § 101 covers devices (machine) as well as compositions, and makes no distinction between the two with regard to meeting the burden of complying with 35 U.S.C. § 101. Furthermore, the case law in question (*Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999)) cites *Brenner v. Manson*, 383 U.S. 519, 534 (1966), which the Examiner obviously believes is not "irrelevant to the instant case", since the Examiner himself cites this exact case three times in the Action (see Action at pages 5, 6 and 7). Additionally, other cases cited by Applicants in the previous response (*Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985) and *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)) do not concern devices, but rather compositions. Thus, this argument completely fails to support the alleged lack of utility of the presently claimed compositions.

Rather, with regard to the utility of the presently claimed sequence, as 60% of the pharmaceutical products currently being market by the entire industry target G-protein coupled receptors (Gurrath, 2001, Curr. Med. Chem. 8:1605-1648), a preponderance of the evidence clearly weighs in favor of Applicants' assertion that the skilled artisan would readily recognize that the presently described sequences have a specific (the claimed GPCR proteins are encoded by a specific locus on the human genome), credible, and well-established utility, for example in tracking gene expression. As set forth in the previous response, as taught in the specification as originally filed, at least at page 33, lines 5-26, the claimed polynucleotide sequence can be used to track the expression of the gene

encoding the described protein. In particular, the specification describes how the described sequence can be represented using a gene chip format to provide a high throughput analysis of the level of gene expression. Such “DNA chips” clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. As the present sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Given the widespread utility of such “gene chip” methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Evidence of the “real world” substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, two such companies (Agilent acquired by American Home Products and Rosetta acquired by Merck) were viewed to have such “real world” value that they were acquired by large pharmaceutical companies for significant sums of money. The “real world” substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science 291:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science 291:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of

human genomic information has been clearly understood for many years). Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 11, line 5, the present nucleotide sequence has a specific utility in “determining the genomic structure” of the allele encoding the presently claimed sequence. This is evidenced by the fact that SEQ ID NO:43 can be used to map 12 coding exons of the gene encoding SEQ ID NO:43 on chromosome 16 (present within a chromosome 16 clone; Genbank Accession Number AC018552; alignment and the first page from the Genbank report are presented in **Exhibit C**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 16 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Applicants respectfully remind the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence, as described above. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). It is well established in the art that such biologically validated splice junctions are superior to splice junctions that may have been predicted from genomic sequence alone. Further, the

specification teaches, at least at page 11, lines 7-11, that “sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics”. Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants’ position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (*supra* at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office (“the PTO”) itself for compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the “real-world” utilities that the Examiner seems to be requiring. Additionally, the Office has recently issued U.S. Patent 6,043,052, which concerns an “orphan” G-Protein coupled receptor identified based only on homology to the orphan

receptor GPR25, similar to the situation with Applicants' currently claimed sequence. Importantly, this issued patent also contains no examples of the "real world" utilities seemingly required in the present case. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section III, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, as well as the reasons set forth in Applicants' response filed on October 28, 2002 to the first Office Action mailed on June 28, 2002, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-3 and 6-9 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

### **III. Rejection of Claims 1-3 and 6-9 Under 35 U.S.C. § 112, First Paragraph**

The Action next rejects claims 1-3 and 6-9 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-3 and 6-9 have been shown to have "a specific, substantial, and credible utility", as detailed in section II above, the present rejection of claims 1-3 and 6-9 under 35 U.S.C. § 112, first paragraph, cannot stand.

For each of the foregoing reasons, as well as the reasons set forth in Applicants' response filed on October 28, 2002 to the first Office Action mailed on June 28, 2002, Applicants request that the rejection of claims 1-3 and 6-9 under 35 U.S.C. § 112, first paragraph, be withdrawn.



#### IV. Rejection of Claims 1-3 and 6-9 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-3 and 6-9 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for the full scope of the claimed invention comprising a genus of at least 22 contiguous nucleotides of SEQ ID NO:43. Applicants respectfully traverse.

Applicants first note for the record that while the rejection of claims 1-3 is allegedly maintained “as set forth at pages 5-7 of the previous Office Action (Paper No. 9, June 28, 2002)” (Action at page 8), the rejection to which the Examiner refers was only applied to claim 1, which concerns a genus of at least 22 contiguous nucleotides of SEQ ID NO:43, and **not** to claims 2 and 3, which does **not** even include the complained of limitation. Applicants therefore respectfully request clarification of this rejection in the next communication from the Office.

The Action then states that claim 1 is not enabled because “(i) there is no evidence that 22 residues are sufficient to retain the functions of the full length (*sic*) and (ii) even if so, there is no guidance regarding which 22 residues are sufficient” (Action at page 10).

Applicants point out that the above comment is **completely irrelevant** to determining whether the claimed compositions meet the legal requirements for patentability under 35 U.S.C. § 112, first paragraph. There is absolutely **no** requirement that all species of an invention must have all of the exact same properties. It is well established that the enablement requirement is met if **any** use of the invention (or in this case, certain species of the invention) is provided (*In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka*, 224 USPQ 739 (Fed. Cir. 1985)). “The enablement requirement is met if the description enables any mode of making and using the invention.” *Johns Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), citing *Engel Indus., Inc. v. Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991). Enablement only requires that the specification describe a practical use for the composition defined in the claims, and that a skilled artisan be able to make and use the claimed DNA segments without undue experimentation. Accordingly, the § 112 requirement has certainly been met.

The Action seems to contend that the specification provides insufficient guidance regarding the biological function or activity of certain of the claimed compositions. However, such an enablement standard conflicts with established patent law. As discussed *In re Brana, supra*, the Federal Circuit admonished the P.T.O. for confusing “the requirements under the law for obtaining a patent with the

requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442.

The Examiner cites *In re Wands, supra*, for the proposition that the present invention could not be practiced without "undue experimentation". However, it is important to remember that in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin, supra*. In *Wands*, the P.T.O. took the position that the applicant failed to demonstrate that the disclosed biological processes of immunization and antibody selection could reproducibly result in a useful biological product (antibodies from hybridomas) within the scope of the claims. In its decision overturning the P.T.O.'s rejection, the Federal Circuit found that Wands' demonstration of success in four out of nine cell lines screened was sufficient to support a conclusion of enablement. The court emphasized that the need for some experimentation requiring, *e.g.*, production of the biological material followed by routine screening, was not a basis for a finding of non-enablement, stating:

Disclosure in application for the immunoassay method patent does not fail to meet enablement requirement of 35 USC 112 by requiring 'undue experimentation,' even though production of monoclonal antibodies necessary to practice invention first requires production and screening of numerous antibody producing cells or 'hybridomas,' since practitioners of art are prepared to screen negative hybridomas in order to find those that produce desired antibodies, since in monoclonal antibody art one 'experiment' is not simply screening of one hybridoma but rather is entire attempt to make desired antibody, and since record indicates that amount of effort needed to obtain desired antibodies is not excessive, in view of Applicants' success in each attempt to produce antibody that satisfied all claim limitations.

*Wands* at 1400. Thus, the need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112, first paragraph. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., supra*.

The Action cites Wallace *et al.* (1987, Methods Enzymol. 152:432-443) for the proposition that "determining the specificity of hybridization is empirical by nature" (Action at page 11). While the relevance of a 13 year old reference to the state of the art at the time of filing of the present application is questionable at best, this argument is again **completely** misplaced, because numerous uses of the claimed sequences do not require knowledge of any hybridization conditions. Applicants point out that

significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling (utilizing, for example, arrays of short, overlapping or non-overlapping, oligonucleotides and DNA chips, as described in Section II, above) to chromosomal mapping (utilizing, for example, short oligonucleotide probes or full length DNA sequences, as described in Section II, above) are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

The Action questions the teaching and guidance in the specification for certain aspects of the present invention. However, as discussed above, this requirement is completely misplaced. There is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design oligonucleotide probes and primers and use them in, for example, PCR based screening and detection methods to obtain the described sequences and/or determine tissue expression patterns. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.* (*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

*In re Marzocchi & Horton*, 169 USPQ 367, 369 (CCPA 1971), emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra*. In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques are routine in the art, such protocols do not need to be described in detail in the specification.

Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. The present claims are thus enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

For each of the foregoing reasons, as well as the reasons set forth in Applicants' response filed on October 28, 2002 to the first Office Action mailed on June 28, 2002, Applicants submit that all aspects of the enablement rejection under 35 U.S.C. § 112, first paragraph have been overcome. Applicants therefore respectfully request that the rejection be withdrawn.

#### **V. Rejection of Claim 1 Under 35 U.S.C. § 112, First Paragraph**

The Action next rejects claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

The Action states that claim 1 fails to meet the written description requirement because it "does not require that the nucleic acid molecules possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature" (Action at page 11). However, the Action admits that claim 1 in fact does include a "conserved structure" and a "distinguishing feature", specifically, that the nucleic acid molecule must include "a stretch of at least 22 consecutive nucleotides of (S)EQ ID NO:43 (Action at page 11). Applicants respectfully point out that this is all that is

required of claim 1 to meet the written description requirement of 35 U.S.C. § 112, first paragraph. As set forth in the previous response, the Federal Circuit has held that an adequate description of a chemical genus “requires a precise definition, such as by structure, formula, chemical name or physical properties” sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; “*Fiers*”). *Fiers* goes on to hold that the “application satisfies the written description requirement since it sets forth the . . . nucleotide sequence” (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

In claims to genetic material ... a generic statement such as ‘vertebrate insulin cDNA’ or ‘mammalian insulin cDNA’, without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function (as seemingly required by the Action), or a method of isolation, but in fact are distinguished by structural features - a chemical formula, i.e., the *sequence itself*.

Using the nucleic acid sequences of the present invention (as set forth in the Sequence Listing),

the skilled artisan would readily be able to distinguish the claimed nucleic acids from other materials on the basis of the specific structural description provided. Polynucleotides comprising at least 22 contiguous bases of nucleotide sequence first disclosed in SEQ ID NO:43 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. Claim 1 thus meets the written description requirement.

For each of the foregoing reasons, as well as the reasons set forth in Applicants' response filed on October 28, 2002 to the first Office Action mailed on June 28, 2002, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, be withdrawn.

## VI. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Li have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

March 17, 2003

Date

David W. Hibler

David W. Hibler  
Agent for Applicants

Reg. No. 41,071

LEXICON GENETICS INCORPORATED  
8800 Technology Forest Place  
The Woodlands, TX 77381  
(281) 863-3399



24231

PATENT TRADEMARK OFFICE